

The Impact of the inflammatory process and biomarkers in recurrent urethral stricture

Biomarkers and the inflammatory process in urethral stricture

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Abstract

Aim: Urethral stricture is a clinical condition characterized by fibrosis of the urethral mucosa, often recurrent, and frequently requiring hospitalization and surgical intervention. Various inflammatory markers, such as the Systemic Inflammatory Index, have been reported to increase in recurrent urethral strictures and be effective in predicting recurrence. This study aimed to evaluate the role of inflammatory processes and markers in patients who underwent internal urethrotomy and to determine their relationship with recurrence.

Materials and Methods: Male patients aged 18–80 years who underwent urethral surgery and had complete data were included in the study. Hemogram parameters, platelet-to-lymphocyte ratio (PLR), neutrophil-to-lymphocyte ratio (NLR), AST/ALT ratio, and patient comorbidities were analyzed. Patients were divided into recurrent and non-recurrent groups after internal urethrotomy.

Results: Recurrence was statistically higher in patients with diabetes mellitus ($p < 0.05$). No significant differences were observed between the groups in laboratory parameters such as WBC, lymphocyte, and platelet counts, or in ratios such as AST/ALT, PLR, and NLR. However, CRP levels were significantly higher in the recurrent group compared to the non-recurrent group ($p < 0.05$).

Discussion: The recurrence rate of urethral stricture was higher in patients with chronic diseases such as diabetes mellitus and hypertension. Our findings suggest that the presence of diabetes mellitus increases the likelihood of recurrence following internal urethrotomy and that elevated CRP levels at admission may be a predictive marker for recurrence.

Keywords

biomarkers, inflammation, urethral stricture, inflammatory markers

Introduction

Urethral stricture is a clinical condition that develops as a result of fibrosis of the urethral mucosa, often recurrent in nature, and frequently requiring hospitalization and surgical intervention [1]. In addition to inflammation, etiological factors include sexually transmitted infections, iatrogenic urethral trauma (such as catheterization), perineal trauma, and a history of prostate surgery [2,3]. The incidence of urethral stricture is reported to be between 23 and 63 per 10,000 individuals, with the most common localization being the bulbar urethra among anterior urethral strictures [4]. Treatment options include internal urethrotomy, urethral dilatation, and open surgery such as urethroplasty [2,4]. Despite a reported success rate of 8–77% for internal urethrotomy, the recurrence rate of urethral stricture remains high [3,4]. One of the reasons for this high recurrence is that internal urethrotomy itself contributes to scar formation [4].

In recent years, inflammation has been shown to be closely associated with urethral stricture, and inflammatory processes are considered significant contributing factors in its pathogenesis [5]. In an experimental rat model of urethral stricture, inflammatory parameters were found to be increased, with a marked and severe inflammatory response demonstrated in the stricture group [5,6]. Furthermore, urethral inflammation and infiltration of inflammatory cells have been identified as key factors in the development of stricture [7]. Elevated inflammatory markers, such as the Systemic Inflammatory Index (SII), have also been reported in recurrent urethral stricture, and these markers may play an important role in predicting recurrence [6]. Several studies have recognized systemic inflammatory markers as reflections of the body's overall inflammatory response [8-16].

Based on this background, the present study aimed to evaluate inflammatory processes and markers in patients who underwent internal urethrotomy for urethral stricture, comparing those with and without recurrence during follow-up, in order to determine their potential role in predicting recurrence.

Materials and Methods

This retrospective study was conducted at the Department of Urology, Aksaray Training and Research Hospital, between January 2022 and January 2025. The study population consisted of male patients over the age of 18 who were diagnosed with urethral stricture and underwent internal urethrotomy.

Inclusion criteria were male patients aged 18–80 years with complete clinical and laboratory data who had undergone urethral surgery. Exclusion criteria included patients with active inflammatory processes due to systemic diseases, those with active infections, patients who underwent internal urethrotomy as an emergency procedure, individuals younger than 18 or older than 80 years, female patients, and patients with incomplete data.

Demographic, clinical, and laboratory data of the included patients were obtained from the hospital information system, electronic medical records, and patient files. Routine laboratory tests, including hemogram parameters, were retrieved from preoperative blood samples. The platelet-to-lymphocyte ratio (PLR) was calculated as the ratio of platelet to lymphocyte

counts, the neutrophil-to-lymphocyte ratio (NLR) as the ratio of neutrophil to lymphocyte counts, and the AST/ALT ratio (De Ritis ratio) as the ratio of aspartate aminotransferase to alanine aminotransferase.

Patients were divided into five groups based on comorbidities: diabetes mellitus (DM), hypertension (HT), coronary artery disease (CAD), chronic obstructive pulmonary disease (COPD), and others. They were further classified into two groups according to recurrence: patients who developed urethral stricture within six months or later after internal urethrotomy (recurrence group) and those who did not (non-recurrence group). Inflammatory markers were compared between the two groups.

The study was conducted in accordance with the principles of the Declaration of Helsinki. Owing to its retrospective design, informed consent was not required.

Statistical Analysis

The data were analyzed using the Statistical Package for the Social Sciences (SPSS) for Windows, version 22.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were used for the demographic characteristics of the patients. The Chi-square test and Mann-Whitney U test were employed to compare the proportions of categorical variables. The association between chronic diseases and recurrence was evaluated using the Chi-square test. Numerical data were expressed as mean ± standard deviation (SD) and minimum–maximum values. A p-value of <0.05 was considered the threshold for statistical significance in all analyses.

Ethical Approval

The study was approved by the Ethics Committee of Aksaray University (Date: 2025-08-14, No: 2025/62).

Results

A total of 79 patients were included in the study, consisting of 41 patients with recurrent urethral stricture (UD) after the first internal urethrotomy and 38 patients without recurrence. The study flow diagram is presented in Figure 1. The mean age of patients in the recurrent UD group was 65.6 ± 16.7 years, which was not significantly different compared to the non-recurrent group (p = 0.134). In the recurrent group, diabetes mellitus (DM)

Table 1. Comparison of demographic characteristics of the patients

Variables	Total (n=79)	Recurrent urethral stricture		P value
		YES (n=41)	NO (n=38)	
Age (year)	64.5 ± 15.2	65.6 ± 16.7	62.1 ± 14.9	0.134
Comorbidity	No	34 (%43.6)	18 (%43.9)	0.199 ^a
	Yes	44 (%56.4)	23 (%56.1)	
DM	22(%28.2)	15(%36.5)	7(18.4)	< 0.05* ^a
HT	18 (%23.1)	10 (%24.4)	8 (%21.1)	0.257 ^a
CAD	17 (%21.5)	8 (%19.6)	9 (%23.6)	0.852 ^a
COLD	3 (%3.8)	2 (%4.8)	1(%2.5)	0.765 ^a
Other	5 (%6.3)	3 (%7.3)	2 (%5.2)	0.295 ^a
CA history	5 (%6.3)	3 (%7.3)	2 (%5.2)	0.295 ^a

DM: Diabetes mellitus, HT: Hypertension, CAD: coronary artery disease, COLD: chronic obstructive lung disease, CPR: cardiopulmonary resuscitation, WBC: White blood count, BUN: blood urea nitrogen, NLR: neutrophil lymphocyte ratio, PLR: platelet lymphocyte ratio, GLR: glucose potassium ratio.*p-value < 0.05, a: Chi-Square Test (n / %),

Table 2. Comparison of laboratory parameters between patient groups

Variables	Total (n=79)	Recurrent urethral stricture		P-value
		YES (n=41)	NO (n=38)	
WBC (×109/L)	8.6±4.7	8.5±3.6	8.7±4.4	0.153
Neutrophils (×109/L)	5.2±5.9	5.7±3.3	5.4±4.9	0.434
Lymphocyte(×109/L)	3.3±2.2	3.2±2.1	3.3±3.1	0.215
Platelet x 109/L	421±278	425±189	394±186	0.312
NLR	2.6±2.1	2.8±1.8	2.5±1.3	0.064
PLR	121±96	129±78	114±65	0.089
AST	20.9±9.1	18.2±9.2	24.1±8.2	0.785
ALT	18.9±11.2	20.1±9.7	18.1±8.1	0.128
CRP	6.5±24	9.7±25	5.4±14	0.04*
AST/ ALT	1.2±0.6	1.1±0.8	1.2±0.9	0.238

WBC: White blood cell, NLR: neutrophil to lymphocyte ratio; PLR: platelet to lymphocyte ratio; AST: ALT: AST/ ALT: CRP: C-Reactive Protein. As a statistical analysis, the Kruskal-Wallis test was used. * =p<0.05 was considered significant. SD: Standard Deviation

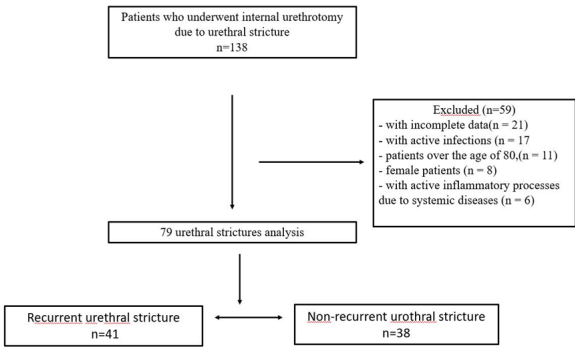


Figure 1. Flowchart for patients undergoing internal urethrotomy due to urethral stricture

was present in 28 patients (68.2%), which was significantly higher compared to the non-recurrent group (p<0.05). The comparison of demographic characteristics between the two groups is summarized in Table 1. No significant differences were observed between the two groups in laboratory parameters such as WBC, lymphocyte, and platelet counts, or in ratios including AST/ALT, PLR, and NLR. However, CRP levels were found to be significantly higher in the recurrent group compared to the non-recurrent group (p < 0.05). The comparison of laboratory values between the two groups is presented in Table 2.

Discussion

Urethral stricture is one of the oldest and most challenging diseases in urology. It is most frequently seen between the ages of 20 and 70, while it is rare outside this age range. This contradicts the notion that the incidence of stricture increases proportionally with age, particularly after the age of 55 [17]. The success of treatment depends not only on the choice of modality but also on the location and length of the stricture [18]. Internal urethrotomy is generally the first-line treatment, whereas open urethroplasty remains the most effective option in recurrent cases. While primary strictures are often idiopathic or iatrogenic, multiple factors contribute to recurrence. Identifying these factors and implementing

preventive measures may reduce recurrence rates. Chronic comorbidities such as diabetes mellitus (DM) and hypertension (HT) have been associated with higher recurrence rates [5]. In our study, we found that DM was a significant factor increasing recurrence after internal urethrotomy, and elevated CRP levels at admission were also higher in the recurrence group. Kinnaird et al. reported in a series of 604 patients that the mean age of patients with recurrent urethral stricture was 44.5 years, and being over 50 years was a risk factor for recurrence [2]. Similarly, Blaschko et al. found the median age of recurrence cases to be 44 (11–75), and Van Dyke et al. reported a mean age of 51.6 years [19,20]. In contrast, the mean age in our study was 65.6 years, which is higher compared to previous studies; this may be related to our exclusion criteria. Chapman et al., in a series of 595 patients who underwent bulbar urethroplasty, identified DM, HT, obesity, and infectious diseases as risk factors for recurrence [21]. Gul et al. also reported that the frequency of DM and HT was higher in patients with recurrent stricture [22]. In line with these studies, we demonstrated that DM was more frequent in patients with recurrence compared to those without recurrence. Bagchi et al., in a study of 105 patients, reported higher CRP levels in patients with recurrent stricture (11.54 ± 3.64) compared to those with successful outcomes [23]. Similarly, Tokuç et al. found that CRP levels in patients with recurrence were 4.5±2.1, nearly twice as high as in non-recurrent cases [24]. Consistent with these findings, our study also showed that CRP levels were significantly elevated in patients with recurrence. Gul et al. reported that PLR, but not NLR, was a risk factor for urethral stricture developing after transurethral resection of the prostate [25]. In contrast, Urkmez et al., in a study of 512 patients with recurrent stricture, found that NLR was elevated and could predict recurrence after surgery [18]. Another study reported that PLR and SII were significant predictors of recurrence, while NLR was not [23]. As seen, no specific inflammatory marker has yet been universally accepted for predicting recurrent urethral stricture. In agreement with this, our study found no significant differences in NLR or PLR between patients with and without recurrence. This study has some limitations. First, it was conducted at a single center with a relatively small sample size, which may limit the generalizability of the findings. Second, due to its retrospective design, certain clinical data could not be fully evaluated. Finally, long-term follow-up data were not available; therefore, late complications could not be assessed. Future studies with larger populations and prospective designs will be necessary to strengthen the clinical utility of inflammatory markers in predicting recurrent urethral stricture.

Limitations

This study has several limitations. First, its retrospective design may have introduced selection bias and limited the ability to establish causal relationships. Second, the sample size was relatively small and derived from a single center, which may restrict the generalizability of the results. Third, only a limited number of inflammatory markers were evaluated; other systemic or local inflammatory parameters that might influence recurrence risk were not assessed. Additionally, the follow-up

duration and patient adherence to postoperative care may have affected recurrence rates. Therefore, larger, prospective, and multicenter studies are needed to confirm these findings and clarify the underlying mechanisms.

Conclusion

In conclusion, urethral stricture is a frequent ailment in men, and more than half of those who undergo internal urethrotomy have a recurrence during follow-up. In our investigation, CRP levels were considerably greater in individuals with recurrent urethral stricture, but other inflammatory markers revealed no significant changes. Furthermore, diabetes mellitus was associated with an increased risk of recurrence. These data imply that increased CRP levels and diabetes mellitus may be objective predictors of recurrence following internal urethrotomy. Prospective, multicenter investigations are required to validate these findings and further understand their therapeutic value.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content, including study design, data collection, analysis and interpretation, writing, and some of the main line, or all of the preparation and scientific review of the contents, and approval of the final version of the article.

Animal and Human Rights Statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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Conflict of Interest

The authors declare that there is no conflict of interest.

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